MC1R, SKIN CANCER AND PHENOTYPIC CHARACTERISTICS

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M-SKIP PROJECT GUIDELINES

This document includes the guidelines, rules, and general conditions applicable to the M-SKIP project. It describes inclusion criteria for studies and participant investigators, rules for data sharing, confidentiality and ownership, use of the data, policy for unpublished studies, publication and authorship. It also includes a description of roles and responsibilities of participants in the project. Please read it carefully and sign it for approval.

M-SKIP study group consists of the following members:

Principal Investigator (PI):	Sara Raimondi, European Institute of Oncology, Milan, Italy
Advisory Committee (AC):	Philippe Autier, IARC, Lyon, France
	Maria Concetta Fargnoli, University of L'Aquila, Italy
	José C. García-Borrón, University of Murcia, Spain
	Jiali Han, Harvard Medical School, Boston, USA
	Peter A. Kanetsky, University of Pennsylvania School of Medicine, Philadelphia, USA
	Maria Teresa Landi, National Cancer Institute, NIH, Bethesda, USA
	Julian Little, University of Ottawa, Canada
	Julia Newton-Bishop, University of Leeds, UK
	Sara Raimondi, European Institute of Oncology, Milan, Italy
	Francesco Sera, ISPO, Florence, Italy
Collaborators (CO)	Saverio Caini, ISPO, Florence, Italy
	Sara Gandini, European Institute of Oncology, Milan, Italy
	Simona Iodice, European Institute of Oncology, Milan, Italy
	Patrick Maisonneuve, European Institute of Oncology, Milan, Italy
Participant Investigators:	all the investigators who send their data for the M-SKIP project.

MC1R, SKIN CANCER AND PHENOTYPIC CHARACTERISTICS

1. Inclusion and exclusion criteria of participant investigators

Investigators who have published or unpublished data from observational studies on single-primary, sporadic melanoma cases or sporadic non-melanoma skin cancer cases with information on any *MC1R* variant will be asked to join the M-SKIP project, as well as investigators with published or unpublished data from control series with information on any *MC1R* variant and phenotypic characteristics under study. Phenotypic characteristics under study will be hair and eye color, skin color, skin type, common and atypical nevi, and freckles.

Papers for which authors could not provide a clear description of genotyping methodology, populations selected for *MC1R* status or for other genetic factors, and studies including only familial skin cancer cases and/or only multiple-primary melanoma cases will be excluded.

Inclusion of unpublished data will depend upon internal peer-review process (see point 6).

2. Rules for data sharing

Investigators who agree to participate in the M-SKIP project will be asked to provide computerized individual data, without personal identifiers. Biological samples are not required; only results of the genetic analyses will be requested. Each investigator will be asked to provide, along with data, a signed statement that the original study had been approved by an Ethic Committee and/or that study subjects signed a written consent to participate in the original study (see also point 9).

Collected data will be stored in a secure computer at the Division of Epidemiology and Biostatics, European Institute of Oncology, Milan, Italy. The data bank will include the data received from the investigators identified at the start of the project, and will be yearly updated with new published and unpublished data.

Under the responsibility of the PI, the data will be checked with quality and logical controls, recoded as to be standardized, and entered in a main data-set.

3. Use of the data

Investigators who agree to join the M-SKIP project consent that their data will be used for pooled-analyses evaluating:

- the association between *MC1R* variants and skin cancer overall, and by skin cancer type;
- the association between *MC1R* variants and phenotypic characteristics under study;

- *MC1R*-phenotype interaction in skin cancer risk, stratified analysis on *MC1R* variants and skin cancer by phenotypic characteristics.

They also consent investigating the role of any other collected factor in confounding or modifying the studied associations.

Beyond the analyses listed above, other studies on the M-SKIP data could be proposed by each member of the M-SKIP study group (PI, AC, CO, and Participant Investigators) following this procedure:

1) The M-SKIP participant sends to the PI a proposal of study with title and a brief protocol including the background, the description of data to be included and expected results.
2) The PI evaluates the feasibility of the project, identifies participant investigators with available data for the proposed study and calculates the statistical power.
3) The PI circulates the proposal to the AC for their approval. The proposal is accepted if approved by the majority of members of the AC.
4) Participant investigators with appropriate data are informed on the ongoing project, and may at this stage decide not let use their data for the specific project within two weeks from the reception of the communication.
5) Under the responsibility of the PI, the data necessary for the approved study are extracted from the main database. Efforts will be made to collect further data useful for the study by investigators who agreed to participate, but who have not send data yet.
6) The final dataset is prepared, and the statistical analysis is carried out in collaboration with the investigator responsible for the approved study.
7) Draft manuscript is circulated to all the coauthors for comments, suggestions, and final approval.

4. Publication policy and authorship

Full authors of each publication will include: the PI; the AC members; every person who significantly contributed to study concept, analysis and interpretation of data, and/or drafting the paper (contributors) and each participant investigator who provided data for that publication.

Generally, the PI of the M-SKIP Project will be the last author. When the PI is the first author, last author will be the participant investigator who provided the largest sample size for that study. When an investigator other than PI proposed a specific study (see point 3) he/she could determine the first and last authorship of that publication. Participant investigators will be

ranked according to the number of subjects included in the study. Members of the AC will be listed in alphabetic order, after participant investigators.

The previous rules apply for publications in scientific journals which do not limit the number of authors. When a maximum number of authors is allowed (for example, for a letter or a short communication), then the investigators directly involved in that paper (significant contributors) will appear as full authors and the remaining participants will be listed as "M-SKIP study group".

5. Roles and responsibilities of M-SKIP participants

The PI is responsible for the conceptual, technical and administrative aspects of the work referred to the M-SKIP project: identifying studies and participant investigators, maintaining contact with participant investigators, collecting, coding and entering data in a central database, supervising data analyses, preparing reports, organizing meetings and drafting manuscripts.

AC is responsible for reviewing/updating the list of investigators to be contacted, approving the scientific documents sent to the investigators, approving the policy for data handling and confidentiality, methods for data analysis, publications, authorship. Moreover, AC members decide whether approving or not new study proposals (see point 3), and participate to the internal peer-review process of unpublished data (see point 6).

CO are responsible for helping the PI in managing and improving the project, and are aware of the status of the project and of the documents sent to investigators.

Participant investigators are responsible of the quality and correctness of their data. They also are responsible for ethical approval of their original study (see point 9).

6. Policy for unpublished data

Unpublished data are both unused data from published studies, including abstract presented at scientific meetings, and data analyzed but never published.

Unpublished data submitted to the M-SKIP project will be evaluated by an internal peer-review process. The data will be sent to the PI, along with the study details: if available, the participant investigator should include a study protocol and/or published *Materials and Methods* section referring to the same study population. The PI and one AC member randomly selected will evaluate the material and data, assess their quality, and decide whether the unpublished data will be included in the M-SKIP data-base or not. During the process, the participant

investigator responsible for unpublished data could be contacted to provide clarification on the data, additional material, and further information.

7. Fundings, equipment and supplies

This project does not require specific funds for data collection and genetic analysis, since this is a pooled-analysis of already gathered data. Participant investigators will be only asked to provide their computerized data and will never be charged with any further expense. Costs of administration, management, and coordination of the project belong to the European Institute of Oncology. Equipment and supplies (computers, licenses for statistical software,…) belong to the European Institute of Oncology as well.

Potential funds provided from future grant applications could help covering: 1) costs related to project management and data analysis, 2) costs related to meeting organization and 3) project-related travel expenses, upon funds availability.

8. Reports and meetings

PI will circulate progress reports of the M-SKIP project among the study group once a year, including information on the participation rate, new identified studies, number of subjects included in the data-base, collected variables, status of the project, ongoing studies, and publications. Annual reports will summarize the results and give in sufficient detail the positive and negative findings so that the value of the work can be assessed.

Upon funds availability, meetings of the AC will be organized once a year and plenary meetings of all the M-SKIP project participants once every two years.

9. Ethics and confidentiality

Each participant investigator shall send, along with data, a signed statement declaring that the original study was approved by an Ethic Committee and/or that study subjects provided a written consent to participate in the original study, and that he/she has permission to exchange anonymized data. Data shall be sent without personal identifiers, only with alphanumerical identification codes. It is the responsibility of each participant investigator to safeguard the rights and welfare of human subjects involved in research, in accordance with the appropriate national code of ethics or legislation, if any, and in the absence thereof, the Helsinki Declaration and any subsequent amendments. If requested by the written informed consent,

each participant investigator is responsible to eventually report the results of this pooled-analysis to the subjects included in the original study.

Collected data will be only used for the purpose of the M-SKIP project as explained at point 3 and will never be disseminated to any other investigator or agency without prior permission of the participant investigator owner of the data.

10. Ownership and cancellation policy

Each participant investigator remains the owner of his/her data. Data sharing will not preclude in any way the investigators from publishing their own data out of the M-SKIP project. Intellectual property rights in the results of the works carried out within the M-SKIP project will be shared among contributing investigators according to specific agreement reached by each approved research protocol. Each participant investigator retains its intellectual property rights over its pre-existing study.

Each investigator could in any moment decide to resign his/her participation in the project by notification to the PI. Moreover, as explained at point 3, each participant investigator may decide not to participate to new study proposals. This will not exclude the investigator of the M-SKIP project in general, but only for that specific study.

I have read the M-SKIP Project guidelines and agree with them.

Date_____

Print name_____

Signature_____